Amendments to the Specification

Please replace the title on page 1, lines 1-2, with the following amended title:

~~HUMAN GENOME-DERIVED SINGLE EXON NUCLEIC ACID PROBES USEFUL FOR GENE EXPRESSION ANALYSIS TWO~~

A Single Exon Nucleic Acid Microarray Useful For Human Gene Expression Analysis

Please replace the paragraph on page 24, line 24, through page 25, line 2, with the following amended paragraph:

Identification can be effected by comparing the genomic sequence returned by query 20 with public or private databases containing known repetitive sequence, vector sequence, artificial sequence, and other artifactual sequence. Such comparison can readily be done using programs well known in the art, such as CROSS_MATCH or REPEATMASKER, the latter available on-line at ~~http://ftp.genome.washington.edu/RM/RepeatMasker.html~~ the RepeatMasker website developed by Smit & Green, or by proprietary sequence comparison programs the engineering of which is well within the skill in the art.

Please replace the paragraph on page 32, line 25, through page 33, line 3, with the following amended paragraph:

For amplification, the putative exons selected in process 300 are input into one or more primer design programs, such as PRIMER3 ~~(available online for use at http://www-genome.wi.mit.edu/cgi-bin/primer/)~~ (Steve Rozen and Helen J. Skaletsky (2000) Primer3 on the WWW for general users and for biologist programmers. In: Krawetz S, Misener S (eds) *Bioinformatics Methods and Protocols: Methods in Molecular Biology.* Humana Press, Totowa, NJ, pp 365-386), with a goal of amplifying at least about 500 base pairs of genomic sequence centered within or about exons predicted to be no more than about 500 bp (or at least about 1000 - 1500 bp of genomic sequence for exons predicted to exceed 500 bp in length) and the primers synthesized by standard techniques. Primers with the requisite sequences can be purchased commercially or synthesized by standard techniques.

Please replace the paragraph on page 35, lines 1-7, with the following amended paragraph:

Robotic spotting devices useful for arraying nucleic acids on support substrates can be constructed using public domain specifications (The MGuide, version 2.0, ~~http://cmgm.stanford.edu/pbrown/mguide/index.html~~ Bioinformatics Resources website, Stanford University), or can conveniently be purchased from commercial sources, such as

the Molecular Dynamics MicroArray Generation III Array Spotter, which is available from Amersham Pharmacia Biotech (Piscataway, NJ, USA). Spotting can also be effected by printing methods, including those using ink jet technology.

Please replace the paragraph on page 49, lines 6-13, with the following amended paragraph:

Although FIG. 3 shows three series of horizontally disposed rectangles in field 81, display 80 can include as few as one such series of rectangles and as many as can discriminably be displayed, depending upon the number of methods and/or approaches used to predict a given function. For example, addition of a fourth gene prediction program, such as GENSCAN ~~(http://genes.mit.edu/GENSCANinfo.html)~~ (GENSCAN web server at the Burge Laboratory at MIT; also see: Burge and Karlin, *J. Mol. Biol.* 268, 78-94 (1997) and Burge, C. B. Modeling dependencies in pre-mRNA splicing signals. In Salzberg, S., Searls, D. and Kasif, S., eds. Computational Methods in Molecular Biology, Elsevier Science, Amsterdam, pp. 127-163 (1998).), to the three gene prediction programs used in our first experiments (GRAIL, GENEFINDER, DICTION) would be accommodated by a fourth series of rectangles disposed horizontally in field 81, but offset vertically from rectangles 81a, 81b, and 81c.

Please replace the paragraph on page 73, lines 9-20, with the following amended paragraph:

For purposes herein, percent identity of two nucleic acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at ~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html~~ the National Center for Biotechnology Information (NCBI) web site. To assess percent identity of nucleic acids, the BLASTN module of BLAST 2 SEQUENCES is used with default values of (i) reward for a match: 1; (ii) penalty for a mismatch: -2; (iii) open gap 5 and extension gap 2 penalties; (iv) gap X_dropoff 50 expect 10 word size 11 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 101, line 26, through page 102, line 2, with the following amended paragraph:

Bacterial cells can be rendered electrocompetent — that is, competent to take up exogenous DNA by electroporation — by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided online in Electroprotocols Online: Collection of

Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~.

Please replace the paragraph on page 103, lines 8-13, with the following amended paragraph:

Protocols for electroporating mammalian cells can be found online in Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~. See also, Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechiques Books, Eaton Publishing Co. (2000) (ISBN 1-881299-34-1), incorporated herein by reference in its entirety.

Please replace the paragraph on page 104, lines 13-25, with the following amended paragraph:

For purposes herein, percent identity of two amino acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at

~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html,~~

the National Center for Biotechnology Information (NCBI) web site. To assess percent identity of amino acid sequences, the BLASTP module of BLAST 2 SEQUENCES is used with default values of (i) BLOSUM62 matrix, Henikoff *et al.*, *Proc. Natl. Acad. Sci USA* 89(22):10915-9 (1992); (ii) open gap 11 and extension gap 1 penalties; and (iii) gap x_dropoff 50 expect 10 word size 3 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 135, lines 14-22, with the following amended paragraph:

Accordingly, after selecting the largest exon per gene bin, a 500 bp fragment of sequence centered on the exon was passed to the primer picking software, PRIMER3 ~~(available online for use at http://www-genome.wi.mit.edu/cgi-bin/primer/)~~ (Steve Rozen and Helen J. Skaletsky (2000) Primer3 on the WWW for general users and for biologist programmers. In: Krawetz S, Misener S (eds) *Bioinformatics Methods and Protocols: Methods in Molecular Biology.* Humana Press, Totowa, NJ, pp 365-386). A first additional sequence was commonly added to each exon-unique 5' primer, and a second, different, additional sequence was commonly added to each exon-unique 3' primer, to permit subsequent reamplification of the amplicon using a single set of "universal" 5' and 3' primers, thus immortalizing the amplicon. The addition of universal

priming sequences also facilitates sequence verification, and can be used to add a cloning site should some exons be found to warrant further study.

Please replace the paragraph on page 150, line 25, through 151, line 4, with the following amended paragraph:

Second, we added Mouse comparative genomics as a fifth gene prediction method, as follows. The UCSC human genome assembly ~~(http://genome.ucsc.edu/)~~ (available on-line at the UC Santa Cruz Genome Bioinformatics website) and finished and unfinished public mouse BAC sequence ~~(http://www.ncbi.nlm.nih.gov/genome/seq/MmHome.html)~~ (available on-line at the Mouse Genome Sequencing website of National Center for Biotechnology Information) were compared using the sequence alignment tool BLAST. Returns were filtered to meet the following requirements: conserved elements greater than 100 bp in length with expect scores less than 0.05 and having an open reading frame (ORF) of greater than 90% of their length. The 100 base pair cutoff was necessary to provide an adequate target for microarray hybridization and the ORF requirement eliminated non-expressed regulatory regions and non-coding RNAs.

Please replace the paragraph on page 185, line 23, through page 186, line 8, with the following amended paragraph:

In other studies, linkages and/or associations of genetic markers with atopy, bronchial hyperresponsiveness and/or asthma have been reported in candidate regions, including the 6p region, which includes both the HLA complex and the Tumor Necrosis Factor a gene (TNF-a), the 11q region which includes the gene coding for the b sub-unit of the high-affinity IgE receptor (FcE R1), the T-cell receptor a gene on chromosome 14, the 5q region bearing numerous candidate genes among which are the interleukin (IL-3, 4, 5, 9, 13) cluster and the b_2-adrenergic receptor gene, the 12q region containing the genes for interferon-gamma (IFNg), a mast cell growth factor (MGF), and an insulin-like growth factor (IGF1). The strongest of these linkages are associated with chromosomes 5 and 11. Other linkage regions have been reported on chromosomes 6, 7, 11, 12 and 13. Demenais, The European Network For Understanding Mechanisms of Severe Asthma, BIOMED 2 Program - European Commission (1998). Linkage regions have also been suggested on chromosomes 3, 16 and 14. Duffy, D., "Review of Molecular Genetics of Asthma and Allergy", ~~(http://www2.qimr.edu.au/davidD/asthma6.html)~~ (available on-line at David Duffy's homepage maintained by the Queensland Institute of Medical Research, Queensland, Australia.